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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/512,736	02/24/2000	Mich B. Hein	TSRI-184.2con4	5292

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EXAMINER

COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
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1638

23

DATE MAILED: 09/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/512,736

Applicant(s)

HEIN ET AL.

Examiner

Cynthia Collins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 13 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 53,56,63-65,67,68 and 76-84 is/are pending in the application.

4a) Of the above claim(s) 77-84 is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 53,56,63-65,67,68 and 76 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☒ Interview Summary (PTO-413) Paper No(s). 18.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed November 13, 2002, paper no.19, has been entered.

Claims 21-52, 54-55, 57-62 and 70-75 have been cancelled.

Claim 53 is newly amended.

Claims 77-84 are newly added.

Claims 53, 56, 63-65, 67-68 and 76-84 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Election/Restrictions

Newly submitted claims 77-84 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 77 recites "wherein said plant cell does not contain nucleotide sequence encoding said antigen specific portion of an immunoglobulin heavy chain", and claims 78-84 depend from claim 77. The restriction requirement mailed July 5, 2002 set forth three groups of inventions: group I drawn to plant cells containing nucleotide sequences encoding both heavy and light chain immunoglobulin polypeptides, group II drawn to plant cells containing nucleotide sequences encoding heavy chain immunoglobulin polypeptides, and group III drawn to plant cells containing nucleotide sequences encoding light chain immunoglobulin polypeptides. Applicant elected the invention of group III, plant cells containing nucleotide sequences encoding light chain immunoglobulin polypeptides. While claims directed to specific immunoglobulin products comprising an abzyme,

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a Fab, a Fab', a F(ab')₂, an Fv and an antibody were also included in group III and were searched examined in the previous office action, claims directed to plant cells that contain both nucleotide sequences encoding heavy chain immunoglobulin polypeptides which lack an antigen specific portion of an immunoglobulin heavy chain and nucleotide sequences encoding light chain immunoglobulin polypeptides were not. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 77-84 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 53, 56, 63-65, 67-68 and 76 are examined on the merits in the instant office action.

Claim Rejections - 35 USC § 112

Claims 53, 63-68 and 76 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's arguments filed November 13, 2002, have been fully considered but they are not persuasive.

Applicant argues that the language "at least a portion of the variable region of an immunoglobulin light chain" cannot be new matter as this language can be found literally or nearly so at multiple sites in the specification, particularly at pages 11, 15, and 16 (reply pages 4-6). Applicant also disagrees that the claim language would encompass polypeptides with as few

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as one amino acid, and points to the claim limitation that requires the expressed polypeptide be capable of forming an antigen-specific immunoglobulin when coexpressed with a heavy chain. Applicants additionally agree that the claim language would encompass polypeptides having at least one amino acid less than a full length, and argue that since a polypeptide having at least one amino acid less than a full length is “at least a portion of the variable region”, the Examiner’s argument does not support a new matter rejection (reply page 6). Applicants also disagree that one skilled in the art would understand Applicant’s disclosure to be limited solely to specific antibody fragments that were known in the art, as the specification discloses that genetic engineering of antibodies was already known in the art prior to Applicant’s filing date (reply pages 6-8).

The Office disagrees that the language “at least a portion of the variable region of an immunoglobulin light chain” can be found literally or nearly so at multiple sites in the specification. The language at pages 11, 15, and 16 refer to immunoglobulin light chain portions in the context of the composition of specific antibody fragments, namely an Fv fragment and an abzyme. With respect to the claim language encompassing polypeptides with as few as one amino acid and the claim limitation that requires the expressed polypeptide be capable of forming an antigen-specific immunoglobulin when coexpressed with a heavy chain, the Office maintains that the limitation “said portion of the variable region of a light chain being capable of assembly with an antigen specific portion of an immunoglobulin heavy chain to form an antigen specific immunoglobulin” does not preclude the claim language from encompassing polypeptides with as few as one amino acid, because the limitation refers to the variable region of the light chain from which the portion was obtained. With respect to the claim language

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encompassing a polypeptide having at least one amino acid less than a full length being equivalent to "at least a portion of the variable region", the Office maintains that the Examiner's argument does support a new matter rejection, as this limitation was not recited in the originally submitted claimed and does not find support elsewhere in the specification. With respect to the disclosure that genetic engineering of antibodies was already known in the art prior to Applicant's filing date, the Office maintains that the specification does not refer to nucleotide sequences "encoding at least a portion of the variable region of an immunoglobulin light chain" in this context.

Claim 53 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "derived", for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's arguments filed November 13, 2002, have been fully considered but they are not persuasive.

Applicant argues that the claim is not indefinite as one skilled in the art would understand that "derived" properly reflects that various lengths of light chain are encompassed under the claim when read in light of the specification (reply page 9).

The Office maintains that the recitation of "derived" renders the claim indefinite as "derived" does not indicate how much of the light chain is "derived" from the antigen specific immunoglobulin and how much of the light chain is retained by the antigen specific immunoglobulin.

Claim Rejections - 35 USC § 102

Claims 53, 56, 63-64, 67-68 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Goodman (US Patent No. 4,956,282, September 11, 1990), for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's arguments filed November 13, 2002, have been fully considered but they are not persuasive.

Applicant argues that Goodman cannot anticipate the claimed invention as Goodman fails to teach a plant cell that contains a nucleic acid encoding at least a portion of a light chain variable region but not a heavy chain, or that the light chain, or portion of a variable region, be capable of forming an antigen-specific immunoglobulin when coexpressed with a heavy chain in a plant cell. Applicant also argues that Goodman's reference to expressing an immunoglobulin extrapolated from a single example is not enabling for antibody expression of a heterodimer, let alone a single immunoglobulin chain. Applicant also points to the Lerner Declaration's assertion that the ability to express an individual light or heavy chain was unexpected, and During's failure to detect light chain expression in plant cells as evidence against the view that the expression of heterologous polypeptides having a leader sequence which is cleaved during proteolytic processing would have been within the limits of one skilled in the art (reply pages 11-12).

The Office maintains that Goodman anticipates the claimed invention. Goodman teaches a plant cell that contains a nucleic acid encoding at least a portion of a light chain variable region but not a heavy chain, as Goodman teaches that the structural genes of interest for practicing his invention include immunoglobulins, "with the structural genes coding for the light and heavy chains" (column 3 lines 20-22). With respect to the limitation that the light chain, or portion of a

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variable region, be capable of forming an antigen-specific immunoglobulin when coexpressed with a heavy chain in a plant cell, the Office maintains that such a capability is an inherent feature of a light chain immunoglobulin. The Office further maintains that the claims are not directed to a plant cell that expresses a heterodimer, but to a plant cell that expresses an individual heterologous polypeptide, and that the expression of an individual heterologous polypeptide would have been within the abilities of one skilled in the art at the time of filing. The Office further maintains that Goodman's expression of a heterologous interferon polypeptide in plant cells would reasonably have been considered to advance the possibility of expressing any single chain heterologous polypeptide in a plant cell.

Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman (US Patent No. 4,956,282, September 11, 1990) in view of Applicant's admitted prior art. for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's arguments filed November 13, 2002, have been fully considered but they are not persuasive.

Applicant points out that independent claim 53 was not included in the rejection, and asserts that there is no legal basis on which to hold claim 65 obvious when independent claim 53 is held nonobvious (reply page 13). Applicant argues that Goodman fails to mention, teach or suggest a plant cell containing a nucleotide sequence encoding at least a portion of the variable region of a light chain but not a heavy chain, and that Goodman is not enabling. Applicant argues that Goodman's teachings would not reasonably have been considered to advance the possibility of expressing at least a portion of the variable region of a light chain but not a heavy

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chain in plants, as gamma interferon is structurally and functionally distinct from immunoglobulin light or heavy chains. Applicant also argues that the gamma interferon polypeptide expressed by Goodman is naturally a single polypeptide whereas an immunoglobulin light chain is naturally a member of a heterodimer. Applicant additionally argues that Goodman fails to teach the claim requirement that the light chain, or portion of a variable region, be capable of forming an antigen-specific immunoglobulin when coexpressed with a heavy chain in a plant cell (reply pages 13-14).

First, the Office maintains that independent claim 53 was not included in the rejection under 35 U.S.C. 103(a) as being unpatentable over Goodman because independent claim 53 was rejected under 35 U.S.C. 102(b) as being anticipated by Goodman. The rejection of claim 53 under 35 U.S.C. 102(b) as being anticipated by Goodman is the legal basis on which to hold claim 65 obvious. Claim 53 is NOT held to be nonobvious over Goodman, claim 53 is held to be anticipated by Goodman. Second, the Office maintains that Goodman teaches a plant cell containing a nucleotide sequence encoding at least a portion of the variable region of a light chain but not a heavy chain and that Goodman is enabling for the expression of a heterologous polypeptide in a plant cell, as discussed *supra* under 35 U.S.C. 102(b). Furthermore, while gamma interferon is structurally and functionally distinct from immunoglobulins, both gamma interferon and immunoglobulins are heterologous to plants. Additionally, while gamma interferon polypeptide expressed by Goodman is naturally a single polypeptide whereas an immunoglobulin light chain is naturally a member of a heterodimer, expression of immunoglobulin light chain in homologous and heterologous systems was known in the art.

Finally, with respect to the limitation that the light chain, or portion of a variable region, be capable of forming an antigen-specific immunoglobulin when coexpressed with a heavy chain in a plant cell, the Office maintains that such a capability is an inherent feature of a light chain immunoglobulin.

Double Patenting

The Office acknowledges receipt of the petition under 37 CFR 1.182 to nullify a terminal disclaimer. Upon the mailing of this office action, this application will be forwarded to the Office of Petitions for disposition of the petition in due course.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Remarks

No claim is allowed.

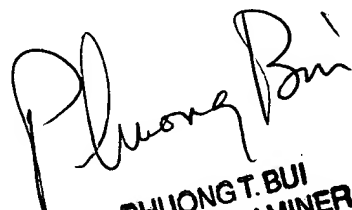
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210.

The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
January 27, 2003


PHUONG T. BUI
PRIMARY EXAMINER

1/27/03